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Abstract: Osteoarthritis is one of the most common causes of lameness and often is a career-ending disease in horses. Treatment of osteoarthritis is usually symptomatic and aimed at controlling the inflammation, either systemically or intra-articularly. Common intra-articular treatments include corticosteroids combined with hyaluronic acid and chondroprotective drugs such as glucosamine and chondroitin. The application of gold compounds, either orally or intramuscularly, has been used therapeutically for many decades, primarily in human patients with rheumatoid arthritis. Gold compounds (aurothiomalate) inhibit the production of nitric oxide (NO) of chondrocytes. Nitric oxide mediates the destructive effects of IL-1 and TNF, which include reduced collagen and proteoglycan production, apoptosis of chondrocytes and stimulation of metalloproteases. The purpose of the present study was to compare the efficacy of the GOLDIC® treatment with that of corticosteroids and hyaluronic acid in horses with arthrogenic lameness. A prospective randomized controlled, two-centre clinical trial was performed. 30 horses with arthrogenic lameness were enrolled in this study. The horses were treated by four injections of gold-induced, autologous conditioned serum GOLDIC® (group B, n = 16) or by a single injection of corticosteroid and hyaluronic acid (group A, n = 14). Lameness was assessed using the AAEP Grading system before and 3, 6, 12 and 36 months after treatment. The AAEP grade was the primary endpoint. Differences were considered significant at $P < 0.05$. Secondary endpoints were the results of the flexion test, degree of joint-effusion, radiographic findings, the ability to return to original performance level and adverse effects. Horses of group B had significantly lower lameness grades at the follow-up examinations compared with the value before treatment ($p < 0.01$). Both treatment groups showed positive effects on the AAEP-Score. Group B (Goldic®) showed much faster effect on the AAEP-Score. Also in the long run group B (Goldic®) showed a larger effect on the AAEP-Score. Severe side effects did not occur in either group. It has been shown that the treatment of arthrogenic lameness in horses with the gold-induced, autologous conditioned serum method (GOLDIC®) is in certain cases a promising alternative to conventional treatment with corticosteroids and hyaluronic acid.

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A prospective comparison of the GOLDIC® technique and corticosteroid plus hyaluronic acid injections for arthrogenic lameness in horses

Anton Fürst¹, Georg Veith² and Josefa Eisenreich²

¹ Equine Department, Vetsuisse-Faculty, University of Zurich, Zurich, Switzerland

² Pferdeklinik Fohlenweide, Königsdorf, Germany

Summary: Osteoarthritis is one of the most common causes of lameness and often is a career-ending disease in horses. Treatment of osteoarthritis is usually symptomatic and aimed at controlling the inflammation, either systemically or intra-articularly. Common intra-articular treatments include corticosteroids combined with hyaluronic acid and chondroprotective drugs such as glucosamine and chondroitin. The application of gold compounds, either orally or intramuscularly, has been used therapeutically for many decades, primarily in human patients with rheumatoid arthritis. Gold compounds (aurothiomalate) inhibit the production of nitric oxide (NO) of chondrocytes. Nitric oxide mediates the destructive effects of IL-1 and TNF, which include reduced collagen and proteoglycan production, apoptosis of chondrocytes and stimulation of metalloproteases. The purpose of the present study was to compare the efficacy of the GOLDIC® treatment with that of corticosteroids and hyaluronic acid in horses with arthrogenic lameness. A prospective randomized controlled, two-centre clinical trial was performed. 30 horses with arthrogenic lameness were enrolled in this study. The horses were treated by four injections of gold-induced, autologous conditioned serum GOLDIC® (group B, n = 16) or by a single injection of corticosteroid and hyaluronic acid (group A, n = 14). Lameness was assessed using the AAEP Grading system before and 3, 6, 12 and 36 months after treatment. The AAEP grade was the primary endpoint. Differences were considered significant at $P < 0.05$. Secondary endpoints were the results of the flexion test, degree of joint-effusion, radiographic findings, the ability to return to original performance level and adverse effects. Horses of group B had significantly lower lameness grades at the follow-up examinations compared with the value before treatment ($p < 0.01$). Both treatment groups showed positive effects on the AAEP-Score. Group B (Goldic®) showed much faster effect on the AAEP-Score. Also in the long run group B (Goldic®) showed a larger effect on the AAEP-Score. Severe side effects did not occur in either group. It has been shown that the treatment of arthrogenic lameness in horses with the gold-induced, autologous conditioned serum method (GOLDIC®) is in certain cases a promising alternative to conventional treatment with corticosteroids and hyaluronic acid.

Keywords: horse, lameness, osteoarthritis, Gold-induced, autologous conditioned serum, GOLDIC®, corticosteroid, hyaluronic acid, IRAP (interleukin-1 receptor antagonist protein), Orthokine, PRP (platelet-rich plasma)

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Correspondence: Prof. Dr. med. vet. Anton Fürst, Equine Department Vetsuisse Faculty University of Zurich, Winterthurerstrasse 260, 8057 Zurich, Switzerland; afuerst@vetclinics.uzh.ch

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Introduction

Degenerative joint disease is very common in humans and in horses (Rossdale et al. 1985, Lawrence et al. 1998, Johnston 1997). In humans, osteoarthritis frequently occurs in elderly patients, but also in young people as a post-traumatic complication (Buckwalter 2003, Buckwalter and Brown 2004). The latter is also a problem in horses because osteoarthritis effects primarily sports horses (McIlwraith 1996). Joint pain impairs normal joint function and severely restricts the quality of life in human and equine patients (Lawrence et al. 1998). Osteoarthritis is one of the most common causes of lameness and often is a career-ending disease in horses (Rossdale et al. 1985), even more so than fatal fractures (Cruz and Hurtig 2008, Pool and Meagher 1990). Abnormal weight-bearing, joint instability and joint infection lead to mechanical and enzymatic damage to the joint cartilage with apoptosis

of chondrocytes and loss of type II collagen and proteoglycans (McIlwraith 1996, Lukoschek et al. 1986, Simmons et al. 1999, Norrdin et al. 1998, Green et al. 2006, Guilak et al. 2004, Buckwalter 1995). Although the main component of the pathogenesis of osteoarthritis is the degeneration of the joint cartilage, the joint capsule and the subchondral bone are also affected (McIlwraith 1996, Cruz and Hurtig 2008, Young et al. 2007). The subchondral bone becomes denser than normal and sclerotic because of large cyclic loads that lead to impaired shock absorption. In addition, shear forces occur at the interface between the subchondral bone plate and mineralised cartilage (McIlwraith 1996, Cruz and Hurtig 2008, Radin and Rose 1986).

The synovial fluid of horses with chronic joint disease has higher levels of tumour necrosis factor (TNF), interleukin 1 (IL-1), IL-6 and prostaglandin E2 (PGE2) than normal horses

(Bertone et al. 2001). The same pro-inflammatory cytokines are also elevated in people with osteoarthritis (Kobayashi et al. 2005). Inflammatory cells of the synovial membrane, synoviocytes and chondrocytes secrete cytokines (Spiers et al. 1994, Clegg et al. 1997a, Clegg et al. 1997b, David et al. 2007, Samuels et al. 2008, Goldring et al. 1988, Loeser 2006, Bondeson et al. 2006) and stimulate the release of metalloproteinase (MMPs) and aggrecanase (Bondeson et al. 2006), as well as other inflammatory mediators like prostaglandins (PGE₂) or nitric oxide (NO) (Guilak et al. 2004, Pelletier et al. 2001, von Rechenberg et al. 2000).

Treatment of osteoarthritis is usually symptomatic and aimed at controlling the inflammation, either systemically or intra-articularly (Caron 2005, Fortier 2005). Common intra-articular treatments include corticosteroids combined with hyaluronic acid (Frean et al. 2002, Schaefer et al. 2009, Trotter 1996) and chondroprotective drugs such as glucosamine and chondroitin (Frean et al. 2002, Frisbie et al. 2009). Intra-articular injection of cytokine inhibitors, which include interleukin 1 receptor antagonists (IL-1Ra) have been used successfully in horses with osteoarthritis (Frisbie et al. 2007) and in humans with osteoarthritis and rheumatoid arthritis (Baltzer et al. 2003, Baltzer et al. 2009, Bresnihan et al. 1998). Orthokine/IRAP therapy involves the intra-articular injection of autologous conditioned serum in which the natural components that block interleukin-1 have been amplified. Incubation of autologous venous blood with chrome sulphate-impregnated glass pearls was shown to amplify the production of anti-inflammatory mediators (Meijer et al. 2003). However, the study by Warner et al. questions the long-term therapeutic success of this treatment (Warner et al. 2016). Another treatment approach is the intraarticular application of Polyacrylamide hydrogel (PAAHG). With this therapy, promising results in the treatment of osteoarthritis of the distal interphalangeal joint could be achieved (Janssen et al. 2012).

The application of gold compounds, either orally or intramuscularly, has been used therapeutically for many decades (Jaeger et al. 2006, Schneider 2011, Schneider and Veith 2013), primarily in human patients with rheumatoid arthritis. Currently, gold salts are administered subcutaneously in the form of gold sticks, and the newest form, termed extra-corporal inductive therapy, consists of gold-induced autologous conditioned serum (GOLDIC®). Gold compounds (aurothiomalate) inhibit the production of nitric oxide (NO) of chondrocytes. Nitric oxide mediates the destructive effects of IL-1 and TNF (Green et al. 2006), which include reduced collagen and proteoglycan production, apoptosis of chondrocytes and stimulation of metalloproteinases (Vuolteenaho et al. 2005). GOLDIC® in vitro studies showed that it not only inhibits catabolic factors, but increases anti-catabolic and anabolic factors. Amongst other things, it could be proved that Gel-solin, key-protein in cell-metabolism, is increased significantly (Schneider 2011). In a large uncontrolled case study that constituted the first report of the clinical application of the GOLDIC® technique, the treatment of horses with different grades of joint disease and lameness resulted in marked improvement in clinical signs (Schneider and Veith 2013). However, the purpose of that study was merely to screen the usefulness of GOLDIC® for the treatment of arthrogenic lameness in horses.

The purpose of the present study was to compare the efficacy of the GOLDIC® treatment with that of corticosteroids and

hyaluronic acid in horses with osteoarthritis. The hypothesis was that both treatments have a therapeutic effect but that the effect of the GOLDIC® treatment is greater.

Material and methods

This clinical study was designed as a prospective randomized controlled lameness trial: The study included horses that were admitted to the Equine Clinic at the Vetsuisse Faculty of the University of Zurich and to the private equine clinic "Fohlenweide" (Heigenkam, Germany) because of lameness attributable to arthropathy. The criteria for inclusion into the study were as follows: the lameness had been present for a minimum of three weeks, the lameness was caused by joint disease diagnosed using nerve blocks and if possible imaging modalities and systemic or intra-articular treatments had not been carried out in the previous three weeks. Horses with conditions amenable to surgical treatment (e.g. osteochondritis) were excluded. After history taking, the horses underwent clinical and orthopaedic examinations. Thirty horses fulfilled the criteria for inclusion into this study, 16 of which were treated with the GOLDIC® method and 14 with betamethasone and hyaluronic acid. The mean age was 12.2 years (range 4 to 18 years) in group A and 10.7 years (2 to 18 years) in group B. The signalment of the horses, the history, the joint affected and adverse effects of treatment are shown in Table 1. Lameness was assessed using the AAEP Grading system (AAEP 2019). The results of the flexion test and the degree of joint effusion were classified as 0 (negative), 1 (mild), 2 (moderate) and 3 (severe). At the end of treatment, the degree of improvement of lameness was assessed.

The different groups were randomized on the basis of a computer-generated list: Group A (Hyaluronic acid/steroid) and Group B (GOLDIC®).

Group A: Horses in this group were given a single intra-articular injection of 12–18 mg betamethasone acetate^a and 20 mg hyaluronic acid^b. The injection site was prepared aseptically, and depending on the temperament of the horse, xylazine^c (0.5 mg/kg) and butorphanol^d (0.02 mg/kg) were given for sedation.

Group B: Horses in this group received 4 ml GOLDIC® activated serum once per week for four weeks using the same injection technique as in group A. The horses underwent clinical examination before each injection, and the degree of joint effusion, swelling and other abnormalities were recorded.

Preparation of GOLDIC®

The gold-induced, autologous-conditioned serum was produced in accordance to the manufacturer's guidelines (Arthro-Gen GmbH). The first injection was performed on day 1 after serum incubation; the other three serum aliquots were stored at –20 °C until the designated day of injection.

Aftercare

After each joint injection, the horses were confined to a box stall for two days, after which time they were hand walked for

Table 1 Codes of the study horses, sex, age, diagnosis, localisation of the arthrogenic lameness, duration of lameness and clinical evaluations of the treated horses. Group A was treated with a single corticosteroid and hyaluronic acid injection, group B with GOLDIC® injections. | Codes der Versuchspferde, Geschlecht, Alter, Diagnose, Lokalisation der arthrogenen Lahmheit, Dauer der Lahmheit und klinische Bewertungen der behandelten Pferde. Gruppe A wurde mit einer einzigen Kortikosteroid- und Hyaluronsäure-Injektion behandelt, Gruppe B mit GOLDIC®-Injektionen.

Group	Age (y)	Sex	Diagnosis	Localisation	Duration	Joint Anesthesia	Return to Function	Adverse Events
A	3	f	Sclerosis third carpal bone	carpal joint front left	weeks	positive	yes	no
A	18	f	hgr OA	tarso-metatarsal joint right	months	positive		no
A	11	m	lgr OA	carpal and carpo-metacarpal joint left	months	positive	no	no
A	7	m	no OA	stifle joint	weeks	positive	no	no
A	10	m	no Rx	tarso-metatarsal joint	weeks	positive	yes	no
A	17	m	mgr OA	fetlock joint left forelimb	weeks	positive	yes	no
A	5	f	no Rx	fetlock joint left forelimb	weeks	positive	yes	no
A	2	m	no Rx	stifle joint	weeks	-	yes	no
A	16	f	lgr OA	pastern joint hind leg right	weeks	positive	?	joint flare after anesthesia
A	17	m	lgr-mgr OA	coffin joint both forelimbs	months	positive	no	no
A	3	f	mgr OA	carpal joint right forelimb	weeks	-	yes	no
A	16	f	lgr OA	fetlock joint right forelimb	months	-	no	no
A	18	m	hgr OA	talocalcaneal joint	weeks	positive	no	no
A	8	f	mgr OA	antebrachio-carpal joint left	weeks	positive		joint flare after anesthesia
B	11	m	cyst femoral condyle	stifle joint	months	positive	no	no
B	18	f	mgr OA	fetlock joint left forelimb	months	-	yes	no
B	12	m	mgr OA	Scapulohumeral joint	months	-	no	no
B	17	f	no OA	coffin joint right forelimb	months	positive	no	increase of lameness for 24 h
B	4	f	no Rx	carpal joint left forelimb	weeks	positive	yes	increased swelling after the first injection
B	8	f	lgr OA	coffin joints both forelimbs	weeks	positive	yes	no
B	5	f	mgr -hgr OA	carpal joint right forelimb	weeks	-		no
B	16	m	mgr OA	coffin joint left forelimb	weeks	positive	yes	no
B	17	m	hgr OA	coffin joint right forelimb	weeks	positive	yes	no
B	18	m	mgr OA	hock right side	months	positive	yes	no
B	6	m	mgr OA	MCG right	months	positive	yes	no
B	10	m	mgr -hgr OA	coffin joint left forelimb	weeks	positive	yes	no
B	18	m	mgr OA	carpal joint right forelimb	months	positive	yes	no
B	10	m	mgr -hgr OA	coffin joint both forelimbs	months	positive	yes	no
B	13	m	mgr OA	coffin joint right side	months	positive	yes	no
B	13	f	mgr -hgr OA	coffin joint right side	months	positive	yes	increased swelling after the second injection

(hgr OA = high grade osteoarthritis; mgr OA = mid grade osteoarthritis; lgr OA = low grade osteoarthritis; Rx = x-ray) | (hgr OA = hochgradige Osteoarthritis; mgr OA = mittelgradige Osteoarthritis; lgr OA = leichtgradige Osteoarthritis; x = Röntgenaufnahme)

the entire duration of the treatment. At the end of the treatment period, exercise was gradually increased depending on the degree of lameness.

Outcome

The main endpoint was the degree of lameness assessed using the AAEP Grading system 3, 6, 12 and 36 months after treatment. Further endpoints were the recovery to the point of full function of the leg, and radiographic findings (osteoarthritis progression).

Power analysis

The number of patients required to detect an effect of the GOLDIC® method was determined based on a previous pilot study (Schneider and Veith 2013). The AAEP lameness grade was the primary endpoint and a decrease in lameness by one grade was considered clinically significant. A sample size of 28 patients was required for 80% power ($\alpha = 0.05$, standard deviation = 1.3) to reject the null hypothesis that both treatments were equal. Therefore, 30 horses were used in the present study.

Statistical analysis

The program Sigma Stat 3.5 was used for statistical calculations. To determine how closely the data fits a normal distribution, we computed a Kolmogorov-Smirnov Goodness of Fit test. The data could not be assumed to be reasonably normally distributed. For further analyzes we used non-parametric statistical tests. For tests within each group (HA+S and GOLDIC®) we used Friedman's Two Way ANOVA of Ranks and Wilcoxon signed Rank Test. For tests between the groups (HA+S and GOLDIC®) we used Mann-Whitney U Test. As Mann-Whitney U Tests between T0 values of both groups (HA+S and GOLDIC®) showed that the two samples are not distributed identically, it was not useful to compare the T1, T2, T3, T4 values directly between the two groups (HA+S and GOLDIC®). We defined DELTA values for T1-T4 as the difference relative to T0 using Mann-Whitney U Test.

Results

All horses showed a marked improvement in their degree of lameness by time. The AAEP scores of all horses are demonstrated in Figure 1.

Both treatment groups have a positive temporal development of the AAEP-Score. Comparison of the different times within each group shows higher differences with lower probabilities for same distribution in group B (GOLDIC®). Also, the DELTA Values are higher in group B (GOLDIC®).

In Figure 1, AAEP-Score Means showed clearly that in group A (HA+S) we have a nearly linear temporal development of the AAEP-Score over all Times T0-T4. In group B (GOLDIC®) we found a much stronger but also nearly linear improvement of

the AAEP-Score over T0-T2. Looking at T0-T4 it seems that we have an asymptotic approach to a minimum value after T2.

In the GOLDIC® group 13 of 16 horses got back to their original performance level while three horses were competing at a lower level than before. In this group, we had 2 drop outs at 12 months. One horse could not be followed after being sold to a new owner. The other horse was euthanized based on the cyst in the treated joint.

On the other side, the control group had 6 horses out of 14, which went back to their original state of performance while five weren't capable of getting back. We had one lost of follow-up after 3 and 6 months based on another disease and 2 further drop-outs after 3 years (the owner of these two horses could not be reached for documentation).

The GOLDIC® group had two horses with radiological progression, but they were still capable of being used in their full and original activity. In both groups, no severe side effects could be seen. Nevertheless, one horse got worse for about one grade for a few days while treatment was done.

The age, sex, radiological morphology and duration of lameness had no effect on the results of treatment.

Discussion

This is the first study of the efficacy of the injections of gold-induced, autologous conditioned serum (GOLDIC®) for the treatment of arthrogenic lameness in horses in a prospective comparative study. Intra-articular injections of a corticosteroid and hyaluronic acid, which is commonly used and well established in veterinary medicine, was used in the control group. Corticosteroids have been used for decades for this purpose and are considered a standard treatment for arthrogenic lameness in veterinary medicine (Frean et al. 2002, Schaefer et al. 2009, Trotter 1996). However, treatment with corticosteroids is strictly symptomatic because it does not affect the aetiology of the disease process. A major drawback is the introduction of crystalline steroidal elements into the joint. Repeated intra-articular injections of corticosteroids can cause irritation of the intra-articular structures because of aggrega-

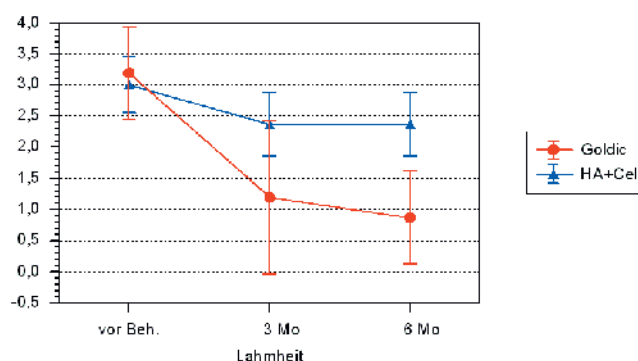


Fig. 1 AAEP lameness scores of all horses in groups A (blue line) and B (red line) before treatment and at follow-up examinations. | AAEP-Lahmheitsbewertungen aller Pferde in den Gruppen A (blaue Säulen) und B (rote Säulen) vor der Behandlung und bei Folgeuntersuchungen.

tion of these crystals (Jones and Doherty 1996, Friedman and Moore 1980, Gaffney et al. 1995).

The treatment of arthrosis with hyaluronic acid is controversial in human medicine (Caborn et al. 2004, Day et al. 2004, Lee et al. 2006, Lundsgaard et al. 2008, Raman et al. 2008, Raynauld et al. 2003, Huang et al. 2011, Juni et al. 2007, Puhl et al. 1993, Qvist et al. 2008, Maheu et al. 2011). Although many studies have investigated this drug a positive effect on damaged joint cartilage has not been demonstrated (Rutjes et al. 2012). Recently, the American Academy of Orthopedic Surgeons published a retraction of a recommendation for the treatment of knee osteoarthritis with hyaluronic acid products based on a meta-analysis (Jevsevar et al. 2013) but hyaluronic acid continues to be used by physicians.

Several novel treatments based on biological processes rather than providing mere pain control have recently been introduced, but the demonstration of efficacy has been difficult (Broeckx et al. 2019). The use of the interleukin-1 receptor antagonist protein (IRAP®), cell-based procedures such as platelet-rich plasma (PRP) and the transplantation of mesenchymal stem-cells have not proven useful for the treatment of degenerative joint disease in horses (Bertone et al. 2014, Ehrle et al. 2013, Fahie et al. 2013, Franklin and Cook 2013). In the daily use, they are often viewed critically (Hildner et al. 2011).

We designed a prospective and controlled study to investigate the effect of the GOLDIC® method for the treatment of arthrogenic lameness in horses with the final follow-up examination at 3 years. This was done to critically examine long-term effects of the treatments. The follow-up period was longer than in other studies that investigated the treatment of arthrogenic lameness.

Both treatments tested in this study led to a decrease in lameness but the effect of the GOLDIC® technique was greater

Table 2 AAEP lameness in groups A and B before treatment and at follow-up examinations (Median values including 25th and 75th percentiles and lost of follow-up | AAEP-Lahmheit in den Gruppen A und B vor der Behandlung und bei Nachuntersuchungen (Medianwerte einschließlich 25. und 75. Perzentil und Verluste bei Nachuntersuchungen)

Group	N	Missing	Median	25%	75%
Goldic pre	16	0	2'000	2'000	3'000
HA+S pre	14	0	3'000	3'000	3'000
Goldic 3mo	16	0	2'000	1'000	2'000
HA+S 3mo	13	1	3'000	2'250	3'000
Goldic 6mo	16	0	1'000	0.000	1'000
HA+S 6mo	13	1	2'000	2'000	3'000
Goldic 12 mo	16	2	0.500	0.000	1'000
HA+S 12mo	13	2	2'000	2'000	2'000
Goldic 3y	16	2	1'000	0.000	1'000
HA+S 3y	12	4	2'000	1'000	2'000

HA+S = Hyaluronic acid and steroids/ HA+S = Hyaluronsäure und Steroide

and statistically significant. Only the horses treated with the GOLDIC® method had significantly lower lameness grades 3 years after treatment than before treatment. The results of the present study are in agreement with another study that also documented significant long-lasting benefits of the GOLDIC® method in the treatment of arthrogenic lameness in horses (Schneider 2011, Schneider et al. 2017).

The mode of action of the GOLDIC® procedure is not well understood. Nevertheless, GOLDIC® has shown in in-vitro studies that plasma Gelsolin could be elevated in the autologous serum significantly (Schneider et al. 2017). Gelsolin is an actin-binding protein and occurs in cells (cytoskeleton) and in plasma (Silacci et al. 2004). The cytoskeleton is responsible for the viscoelasticity of this cells (Trickey et al. 2004). Furthermore, important functions of cells are regulated by Gelsolin: Cell motility, phagocytosis, apoptosis and the activation of thrombocytes (Silacci et al. 2004). The concentration of Gelsolin in plasma is decreased according to different tissue degenerating diseases (Suhler et al. 1997). Experiments have shown decreased plasma Gelsolin concentrations in animals with sepsis, and treatment with Gelsolin had a positive effect on the survival rate in these animals (Lee et al. 2007). Plasma Gelsolin serves as a buffer to intercept inflammatory reactions of the body (DiNubile 2008) and was found to be decreased in rheumatic arthritis (Osborn et al. 2008).

It was beyond the scope of this study to collect serum and synovial fluid samples for measurements of Gelsolin in response to the GOLDIC® treatment. A clinical study of human osteoarthritis in knee joints showed that intra-articular

Table 3 Statistical analysis of the AAEP lameness grades score at different follow-up examinations demonstrated by differences of ranks, Q values and P values. | Die statistische Analyse der AAEP-Lahmheitsgrade ergab bei den verschiedenen Folgeuntersuchungen Unterschiede in den Rängen, Q-Werten und P-Werten

Comparison	Diff. of Ranks	Q	P	P < 0.050
Goldic pre vs Goldic > 3 y	62'955	4'464	<0.001	Yes
Goldic pre vs Goldic > 6 mo	62'277	4'416	<0.001	Yes
Goldic pre vs Goldic 3–6	56'531	4'149	0.002	Yes
HA+S < 3mo vs Goldic > 3 y	76'268	5'031	<0.001	Yes
HA+S < 3mo vs Goldic > 6 mo	75'589	4'986	<0.001	Yes
HA+S < 3mo vs Goldic 3–6	69'844	4'746	<0.001	Yes
HA+S 3–6 vs Goldic > 3 y	63'101	4'162	0.001	Yes
HA+S 3–6 vs Goldic > 6 mo	62'423	4'117	0.002	Yes
HA+S 3–6 vs Goldic 3–6	56'677	3'851	0.005	Yes
HA+S pre vs Goldic < 3mo	48'214	3'419	0.028	Yes
HA+S pre vs Goldic > 3 y	81'857	5'620	<0.001	Yes
HA+S pre vs Goldic > 6 mo	81'179	5'573	<0.001	Yes
HA+S pre vs Goldic 3–6	75'433	5'349	<0.001	Yes
HA+S < 3mo vs Goldic < 3mo	42'625	2'896	0.170	No
HA+S > 6 vs Goldic > 3 y	50'597	3'259	0.050	No
HA+S pre vs HA+S > 3 y	43'589	2'552	0.482	No

treatment with gold-activated serum (GOLDIC®) resulted in a significant increase of Gelsolin in synovial fluid (Schneider 2011).

One limitation of this study was the low number of cases and the heterogeneity of joints affected. Still, in this study, the intra-articular treatment of arthrogenic lameness in horses with the GOLDIC® method yielded significantly better short- and long-term results than the traditional treatment with corticosteroids and hyaluronic acid. Further studies are needed to substantiate whether the beneficial effect of the GOLDIC® method is attributable to an increase in the actin-binding protein, Gelsolin, in synovial fluid.

Manufacturer's addresses

- ^a Celestone-Chronodose®, Essex Chemie, Switzerland
- ^b SynovaMed AG, Liechtenstein
- ^c Xylazin® Streuli Pharma Switzerland
- ^d Alvegesic® 10%, Virbac Switzerland
- ^e Arthrogen med vet GmbH, Germany

Animal welfare statement

This study was approved by the veterinary office of the Canton of Zurich (4312/9.3.2010).

Conflict of interest

The authors declare that they have no conflict of interest. Anton Fürst is member of the Medical board of Arthrogen GmbH but does not have any financial benefits based on this membership.

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